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| 10/585,286 | 07/03/2006 | Sunil Shaunak | GRT/37-93 | 2614 |
| 23117 | 7590 | 04/11/2011 | EXAMINER | |
| NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203 | | | | LAU, JONATHAN S |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/585,286 | SHAUNAK ET AL. |
| | Examiner | Art Unit |
| | Jonathan Lau | 1623 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 7 Feb 2011.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 78-94 and 98-101 is/are pending in the application.
 4a) Of the above claim(s) 91,94 and 101 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 78-90,92,93 and 98-100 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 7 Feb 2011, in which claims 78, 83-86 and 89 are amended to change the scope and breadth of the claim, new claims 98-101 are added, withdrawn claims 95-97 are canceled and withdrawn claims 91 and 94 are amended.

This application is the national stage entry of PCT/GB05/00039, filed 7 Jan 2005; and claims benefit of foreign priority document UNITED KINGDOM 0400264.8, filed 7 Jan 2004; this foreign priority document is in English.

Claims 78-94 and 98-101 are pending in the current application. Claims 94 and new claim 101, drawn to non-elected inventions, are withdrawn. Claim 91, drawn to non-elected species, is withdrawn. Claims 78-90, 92, 93 and 98-100 are examined on the merits herein.

Election/Restrictions

New claim 101 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, the invention of Group II, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 25 Mar 2010.

Rejections Withdrawn

Applicant's Amendment, filed 7 Feb 2011, with respect to claims 78-88 rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as amended claim 78 does not recite polymer comprising units derived from an acrylic acid and amended claim 83 find antecedent basis in amended claim 78. Claims 79-88 depend from claim 78 and incorporate all limitations therein.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 7 Feb 2011, with respect to claims 78-88 and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by Brocchini et al. (WIPO Publication WO 01/18080 A1, published 15 Mar 2001, provided by Applicant in IDS mailed 03 July 2006) has been fully considered and is persuasive, as amended claim 78 requires a substance that has pharmacological activity against a pathogenic organism and Brocchini et al. discloses anti-cancer agents.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 7 Feb 2011, with respect to claims 78-90 and 92 rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (WIPO Publication WO 01/18080 A1, published 15 Mar 2001, provided by Applicant in IDS mailed 03 July 2006) has been fully considered and is persuasive, as amended claim 78 requires a substance that has pharmacological activity against a pathogenic organism and Brocchini et al. teaches anti-cancer agents.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 7 Feb 2011, with respect to claims 78-90, 92 and 93 rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (WIPO Publication WO 01/18080 A1, published 15 Mar 2001, provided by Applicant in IDS mailed 03 July 2006) and in view of Norimov et al. (Bulletin of Experimental Biology and Medicine, 1991, 111(2), p216-218, cited in PTO-892) and Kreuter et al. (Infection and Immunity, 1978, 19(2), p667-675, provided by Applicant in IDS mailed 03 July 2006) has been fully considered and is persuasive, as amended claim 78 requires a substance that has pharmacological activity against a pathogenic organism and Brocchini et al. in view of Norimov et al. and Kreuter et al. teaches the antigen tuberculin.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 7 Feb 2011, with respect to claims 78-90 and 92 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 5, 6, 8, 12, 35, 43, 47, 48 and 49 of U.S. Patent No. 6,803,438 has been fully considered and is persuasive, as amended claim 78 requires a substance that has pharmacological activity against a pathogenic organism and claims 1, 3, 4, 5, 6, 8, 12, 35, 43, 47, 48 and 49 of U.S. Patent No. 6,803,438 are drawn to the (meth)acrylic acid polymer conjugate of anti-cancer agents doxorubicin, daunomycin or paclaxitel.

This rejection has been **withdrawn**.

The following are new or modified grounds of rejection necessitated by Applicant's Amendment, filed 7 Feb 2011, in which claims 78, 83-86 and 89 are amended to change the scope and breadth of the claim, new claims 98-101 are added.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

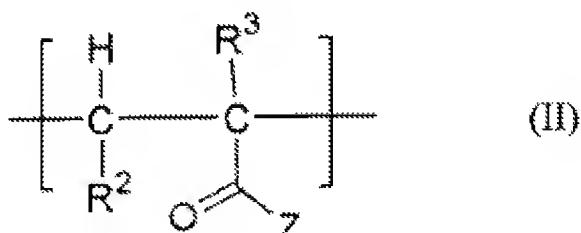
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 78-90, 92, 98 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (WIPO Publication WO 01/18080 A1, published 15 Mar 2001, provided by Applicant in IDS mailed 03 July 2006) and in view of Kuzuya et al. (US Patent 5,889,078, issued 30 Mar 1999, provided by Applicant in IDS mailed

03 July 2006). Junior et al. (WIPO Publication WO 03/039435, published 15 Mar 2003, provided by Applicant in IDS mailed 03 July 2006) provides evidence of inherency.

Brocchini et al. discloses an acrylic acid polymer drug conjugate wherein the polymer has a polydispersity of preferably less than 1.2 and a molecular weight of less than 100,000 (abstract). Brocchini et al. discloses the embodiment within the polymer



comprises the unit (II) wherein R² includes hydrogen or C₁-C₁₈ alkyl, R³ includes hydrogen and Z includes the groups OR⁷ where R⁷ includes hydrogen (page 18 lines 20-30 and page 19, lines 1-5). Brocchini et al. teaches preferably R² is selected from a group including hydrogen and C1-C6 alkyl and most preferably R² is hydrogen and R³ is hydrogen or methyl (page 19, lines 10-15). Brocchini et al. discloses the drug or bioactive agent is preferably an anti-cancer agent such as daunomycin (page 19, lines 25-30). Brocchini et al. discloses the polymer having a molecular weight of less than 100,000 and more preferably 25,000-40,000 (page 18, lines 15-20), meeting limitations of instant claims 87 and 88. Brocchini et al. discloses the acrylic acid polymer drug conjugate as a covalently bonded conjugate. However, as previously detailed, the specification at page 10, lines 8-15 also defines the term "complex" to include that "Although a complex according to the present invention predominantly involves non-covalent association between the components, there may nevertheless be some covalent bonding." and one of ordinary skill in the art

would understand that due to the proximity of the covalently bound drug to the acrylic or methacrylic polymer the drug would necessarily also non-covalently interact by one or more of ionic, electrostatic and van der Waals forces with the acrylic or methacrylic polymer, therefore the “complex” as recited in the instant claims encompasses the covalently bonded conjugate. Brocchini et al. discloses the polymer drug conjugate in a pharmaceutical composition (page 17, lines 5-10), such as with a pharmaceutically acceptable excipient (page 50, lines 20-25), or a carrier, meeting limitations of instant claim 92.

Brocchini et al. does not specifically teach the elected species of a substance that has a pharmacological activity against a pathogenic organism of amphotericin B (instant claims 79-83).

Kuzuya et al. teaches a polymer of acrylic acid or methacrylic acid combined with a drug (abstract). Kuzuya et al. teaches drugs that are compatible with the acrylic acid or methacrylic acid polymer include amphotericin B (column 2, line 30). Junior provides evidence of inherency that amphotericin B (Junior et al. abstract) can be used to treat leishmaniasis (Junior et al. page 11, lines 10-20)

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Brocchini et al. in view of Kuzuya et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teaching of Brocchini et al. to practice the invention wherein the polymer is poly(methacrylic acid). One of ordinary skill in the art would have been motivated to select the teaching of Brocchini et al. with a reasonable expectation of success because

Brocchini et al. teaches guidance for selecting the preferred R groups. It would have been obvious to one of ordinary skill in the art to substitute the drug taught by Brocchini et al. for the drug amphotericin B taught by Kuzuya et al. with a reasonable expectation of success because both Brocchini et al. and Kuzuya et al. teach acrylic acid or methacrylic acid polymer drug conjugates. While Brocchini et al. teaches the drug or bioactive agent is preferably an anti-cancer agent, Brocchini et al. does not appear to teach away from the broader disclosure of drugs or bioactive agent. See also MPEP 2123 II.

Response to Applicant's Remarks:

Applicant's Remarks, filed 7 Feb 2011, have been fully considered and not found to be persuasive.

Applicant notes that the complexes are well known in the art. Liu at page 112, paragraph 4 defines a molecular complex as formed by non-covalent interactions. However, Liu at page 112, paragraph 5 acknowledges that the classification of complexes into various types is somewhat arbitrary, and they can also be classified based on the nature of interaction forces. Further, the ordinary definition of a complex in the chemical arts is "A substance formed by the combination of simpler substances, esp. one in which the bonds between the substances are weaker than or of a different character from those between the constituents of each substance." (definition 1c. of complex, Oxford English Dictionary, cited in PTO-892). As noted by Applicant, this art-known definition is consistent with the definition within the instant specification. However, recited above, the definition within the specification does not exclude covalent

bonding. The ordinary definition of complex states a complex is especially one in which the bonds between the substances are weaker than or of a different character from those between the constituents of each substance, but exemplary qualifier "especially" does not mean the definition excludes covalent bonds between the substances, or bonds between the substances that are of the same character from those between the constituents of each substance. The instant claims encompass all forms of complex as defined by the instant specification. The limitation of a non-covalent complex is not explicitly recited in the claims, nor is such meaning assigned to the term clearly set forth in the specification. Therefore the scope of the invention as recited in the claims, understood in terms defined by the specification and understood within the art, encompasses the covalently-bound complex taught by Brocchini et al. in view of Kuzuya et al.

Amended Claims 93 and 100 rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (WIPO Publication WO 01/18080 A1, published 15 Mar 2001, provided by Applicant in IDS mailed 03 July 2006) and in view of Kuzuya et al. (US Patent 5,889,078, issued 30 Mar 1999, provided by Applicant in IDS mailed 03 July 2006) as applied to claims 78-90, 92, 98 and 99 above, and further in view of Neely et al. (Eur. J. Clin. Microbiol. Infect. Dis. 2000, 19, p897-914, cited in PTO-892).

Brocchini et al. in view of Kuzuya et al. teach as above.

Brocchini et al. in view of Kuzuya et al. does not specifically teach the composition further comprising a delivery system adjuvant (instant claims 93 and 100).

Neely et al. teaches current therapy for treating fungal infections is generally limited to amphotericin B in its parent and lipid formulations and the need for new therapies is pressing (abstract). Neely et al. teaches encapsulation of amphotericin B within lipid is now being applied to enhance the bioavailability of the drug (page 905, left column, paragraph 2). Encapsulation within lipid, or a liposome, is interpreted as a delivery system adjuvant based on the instant specification at page 3, lines 1-5. Neely et al. further teaches the use of combinations of antifungal drugs with adjuvants like FK506 (page 904, left column, paragraph 2), an immune potentiator (page 903, right column, paragraph 3), as a novel treatment strategy.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Brocchini et al. in view of Kuzuya et al. and further in view of Neely et al. One of ordinary skill in the art would have been motivated to combine Brocchini et al. in view of Kuzuya et al. and further in view of Neely et al. with a reasonable expectation of success in order to improve invention of Brocchini et al. in view of Kuzuya et al. comprising amphotericin B in the same way as taught by Neely et al. by including a delivery system adjuvant such as a liposome or an adjuvant such as FK506.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 78-90, 92, 98 and 99 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 5, 6, 8, 11, 35, 47, 48 and 49 of U.S. Patent No. 6,803,438 in view of Kuzuya et al. (US Patent 5,889,078, issued 30 Mar 1999, provided by Applicant in IDS mailed 03 July 2006).

U.S. Patent No. 6,803,438 corresponds to Brocchini et al. (WIPO Publication WO 01/18080 A1). Claims 1, 3, 4, 5, 6, 8, 11, 35, 47, 48 and 49 of U.S. Patent No. 6,803,438 are drawn to the covalently-bonded acrylic acid polymer drug conjugate as detailed above.

Claims 1, 3, 4, 5, 6, 8, 11, 35, 47, 48 and 49 of U.S. Patent No. 6,803,438 in view of Kuzuya et al. teaches as detailed above with regard to Brocchini et al. in view of Kuzuya et al.

Response to Applicant's Remarks:

Applicant's Remarks, filed 7 Feb 2011, have been fully considered and not found to be persuasive.

Regarding the modified grounds of rejection necessitated by Applicant's amendment, the scope of the instantly claimed complex is interpreted to encompass the covalently-bonded acrylic acid polymer drug conjugate taught by claims 1, 3, 4, 5, 6, 8, 11, 35, 47, 48 and 49 of U.S. Patent No. 6,803,438 in view of Kuzuya et al.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan Lau whose telephone number is (571)270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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